CardioMEMS™ HF System

Pulmonary Artery (PA) Pressure-Guided Therapy for Heart Failure Management

The CardioMEMS™ HF System is the first and only FDA-approved heart failure (HF) monitor proven to significantly reduce HF hospital admissions and improve quality of life in NYHA class III patients.

When used by clinicians to manage HF, the CardioMEMS HF System is:

- **Safe and reliable** – 98.6% of patients were free from device or system complications\(^1\)
- **Clinically proven** – reduced HF admissions by 37%\(^1\)
- **Proactive and personalized** – patient management through direct monitoring of PA pressure and titration of medications

Traditional physiologic markers in the development of acute decompensation in patients suffering from HF such as intrathoracic impedance, weight, blood pressure and symptoms are late and unreliable\(^2,3\) with only moderate sensitivity and specificity.\(^4-6\) Large randomized controlled studies using telemonitoring of these indirect markers have failed to reduce HF hospitalizations.\(^2,3,7\) This clinical compendium summarizes key studies demonstrating the safety and efficacy of the CardioMEMS HF System.
PA PRESSURE-GUIDED THERAPY REDUCES HEART FAILURE HOSPITALIZATIONS AND IMPROVES QUALITY OF LIFE IN PATIENTS WITH REDUCED OR PRESERVED EJECTION FRACTION

The CardioMEMS™ HF System monitors PA pressure measurements from a sensor implanted into the pulmonary artery. The safety and accuracy of the CardioMEMS™ PA Sensor has been demonstrated in previous studies.8,9 Systolic and diastolic PA pressures were significantly correlated between the CardioMEMS PA sensor and traditional Swan-Ganz catheter measurements, and between the CardioMEMS PA sensor and standard echocardiography.8,9 A feasibility study reported the safe and successful implantation of the CardioMEMS PA sensor in a clinical setting with no serious device-related events (n=17).9 These preliminary studies provided the safety and accuracy data needed for the pivotal CHAMPION clinical trial and subsequent sub-analyses that support the use of the CardioMEMS HF System to proactively guide HF management in NYHA Class III patients with reduced or preserved left ventricular ejection fraction (LVEF).

Key takeaways:

- The treatment group required <1 medication changes per patient per month compared to the control group (9.1 ± 7.4 vs. 3.8 ± 4.5 changes per patient during first 6 months of follow-up, p<0.0001).

- During the entire follow-up (mean 15 months), PA pressure-guided therapy (treatment group) significantly reduced HF hospitalizations by 37% compared to the control group (p<0.0001, see Figure 1).

- The treatment group had a lower risk of death or freedom from first HF hospitalization during the entire follow-up period compared to the control group (p=0.0086).

Wireless Pulmonary Artery Haemodynamic Monitoring in Chronic Heart Failure: A Randomised Controlled Trial


- The aim of this randomized, multicenter, single-blind, controlled study was to evaluate the safety of the system and the efficacy of PA pressure-guided therapy on HF hospitalizations.

- NYHA Class III HF patients irrespective of LVEF and who had been hospitalized for HF within the past 12 months were implanted with the CardioMEMS PA sensor (n=550); patients were randomized to either the treatment group (HF management guided by PA pressure measurements, n=270), or the control group (standard of care management, n=280).

- Mean follow-up time was 15 months.

- Both primary safety and efficacy endpoints were met:
  - Patients had a 98.6% freedom from device or system-related complications (95% CI 97.3-99.4) with no pressure-sensor failures (95% CI 99.3-100.0).
  - The rate of HF hospitalizations at 6 months was reduced by 28% in the treatment group (p=0.0002).

- During the first 6 months of follow-up, compared to the control group, the treatment group had:
  - A greater reduction in PA pressure (-156 vs. 33 mean area under the curve, p<0.008).
  - Fewer patients admitted to the hospital for HF (20% treatment group vs. 29% control group, p<0.03).
  - More days alive outside of the hospital (174.4 ± 31.1 vs. 172.1 ± 37.8 days, p<0.02).
  - Better patient quality of life (45 ± 26 vs. 51 ± 25, p=0.02 based on Minnesota Living with Heart Failure Questionnaire).

Figure 1. Cumulative heart failure hospitalizations during the entire period of follow-up

- Hazard ratio 0.63 (95% CI 0.53-0.77) p < 0.0001

- 37% RRR p < 0.0001

- 28% RRR p < 0.0002

- 45% RRR p < 0.0001
CardioMEMS Heart Sensor Allows Monitoring of Pressures to Improve Outcomes in NYHA Class III Heart Failure Patients (CHAMPION) Trial: Impact of Hemodynamic Guided Care on Patients with Preserved Ejection Fraction


- This sub-analysis of the CHAMPION clinical trial evaluated the effect of PA pressure-guided therapy with the CardioMEMS HF System in NYHA Class III patients with preserved ejection fraction (HFpEF).
- Of the HFpEF patients (n=115), 59 were randomized to the treatment group (PA pressure-guided therapy) and 56 to the control group (standard of care).

**Key takeaway:**
- PA pressure-guided therapy significantly reduced HF hospitalizations for HFpEF patients in the treatment group by 50% and 60% compared to those patients in the control group at 6 and 15 months, respectively (p<0.0001 and p<0.0004, respectively).

Effect of CRT on Heart Failure Related Hospitalizations in Patients with Reduced EF Utilizing Remote Pulmonary Artery Pressures in the CHAMPION Trial


- This sub-analysis of the CHAMPION clinical trial evaluated the effect of PA pressure-guided therapy with the CardioMEMS HF System in patients with reduced ejection fraction (rEF <40%, n=430) with and without a cardiac resynchronization therapy (CRT) device.
  - 40% (171 of 430) of rEF patients had CRT devices; of this cohort, 82 patients were in the treatment and 89 in the control group.
  - 60% (259 of 430) of rEF patients did not have CRT devices; of this cohort, 126 patients were in the treatment group and 42 in the control group.

**Key takeaways:**
- Remote PA pressure data in the treatment group resulted in similar reductions in HF hospitalization in patients with and without a CRT device, suggesting that HF management guided by PA pressures may provide additive benefits to CRT therapy.
  - For patients in the rEF-CRT group, those who received PA pressure-guided therapy had significantly fewer HF hospitalizations (RRR = 24%, p=0.0264).
  - For patients in the rEF-no CRT group, PA pressure-guided therapy resulted in an RRR = 23%.

Targeting Pulmonary Artery Pressures in the Treatment of Chronic Heart Failure: Insights from the CHAMPION Trial


- This CHAMPION clinical trial sub-analysis determined if remote access to PA pressure data may provide a method to identify and treat high filling pressures in HF patients at increased risk for decompensation (n=550).
- At implant, the mean PA pressure was similar in both control and treatment groups (31.8 ± 10.7 and 31.3 ± 11.1 mmHg, respectively).
- Average PA pressures increased during the 6 weeks prior to HF hospitalizations in both groups (p<0.0001) and decreased significantly after successful in-hospital decongestion (p<0.0001).
- Treatment patients with HF hospitalizations had lower pressures compared to control patients with HF hospitalizations at all timepoints prior to hospitalization.
  - Treatment patients also had lower PA pressures compared to the control patients regardless of hospitalization type (HF-related or non-HF related).

The Malignant Effect of Acute Decompensation in Patients with Chronic Heart Failure: Insights from the CHAMPION Trial


- This CHAMPION clinical trial sub-study reports on the impact of obtaining remote PA pressure data and the effect on patient mortality and quality of life (n=550).
- Patients in both treatment (n=270) and control (n=280) groups who did not experience a HF hospitalization had a 66% reduction in mortality (HR 0.34, 95% CI 0.22-0.54, p<0.0001).
- The treatment group had a significant 27% reduction in the risk of HF hospitalization or death (HR 0.73, 95% CI 0.57-0.94, p=0.015).
- Among patients who did not experience a HF hospitalization, those in the treatment group had an improved quality of life compared to those in the control group (Minnesota Living with Heart Failure Questionnaire, 43.2 vs. 48.9, p=0.0377).

**Key takeaway:**
- The PA pressure monitoring system may reduce the risk of HF hospitalization and mortality while improving a patient’s quality of life.
PA PRESSURE-GUIDED THERAPY HAS BEEN SHOWN TO CONSISTENTLY REDUCE HF HOSPITALIZATIONS IN PATIENTS WITH COMMON HEART FAILURE COMORBIDITIES

HF is often associated with a variety of comorbidities such as respiratory disease, coronary artery disease and atrial fibrillation. These comorbidities contribute to disease progression and may alter the response to treatment. This section highlights additional sub-analyses from the CHAMPION clinical trial that consistently show that PA pressure-guided therapy reduces HF hospitalizations in patients with common HF comorbidities. Table 1 summarizes the rate of HF hospitalizations across the different studies.

<table>
<thead>
<tr>
<th>COMORBIDITY</th>
<th>N SIZE (CONTROL)</th>
<th>N SIZE (TREATMENT)</th>
<th>HF HOSPITALIZATION RATE REDUCTION AT 15 MONTHS IN TREATMENT GROUP</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of myocardial infarction</td>
<td>137</td>
<td>134</td>
<td>46% (p&lt;0.001 vs. control)</td>
</tr>
<tr>
<td>COPD16,17</td>
<td>96</td>
<td>91</td>
<td>41% (p=0.0009 vs. control)</td>
</tr>
<tr>
<td>Pulmonary hypertension18</td>
<td>163</td>
<td>151</td>
<td>36% (p=0.0002 vs. control)</td>
</tr>
<tr>
<td>AF19</td>
<td>135</td>
<td>120</td>
<td>41% (p=0.0001 vs. control)</td>
</tr>
</tbody>
</table>

Table 1: Patients with common HF comorbidities have consistent reduction in HF hospitalizations with PA pressure-guided therapy

The Utility of Remote Wireless Pulmonary Artery Pressure Monitoring in Patients with or without a History of Myocardial Infarction: Experience from the CHAMPION Trial

Strickland WL, et al. JACC 2011.15

- This sub-analysis of the CHAMPION clinical trial determined if PA pressure monitoring affected the clinical outcomes of patients with and without a history of myocardial infarction (MI).
- 271 of the 550 NYHA Class III HF patients enrolled in the CHAMPION clinical trial had a history of MI and were randomized to either the control (n=137) or treatment (n=134) groups.
- At 6 months, there was a 2.2-day benefit of days alive outside the hospital for patients in the treatment group; at 15 months, this increased to 30.1 days.

Key takeaway:
- At 6 months and for the full study duration (mean 15 months), remote PA pressure monitoring had a significant reduction in HF hospitalizations for patients with and without a history of MI in the treatment group versus control (see Table 2).

<table>
<thead>
<tr>
<th>COMORBIDITY</th>
<th>RRR at 6 months for treatment group</th>
<th>RRR at 15 months for treatment group</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of MI</td>
<td>30%, p&lt;0.0039 vs. control</td>
<td>46%, p&lt;0.0001 vs. control</td>
</tr>
<tr>
<td>No MI</td>
<td>25%, p=0.016 vs. control</td>
<td>23%, p=0.021 vs. control</td>
</tr>
</tbody>
</table>

Impact of Wireless Implanted Pulmonary Artery Pressure Monitoring System in Heart Failure Patients with Comorbid Chronic Obstructive Pulmonary Disease


- The purpose of this CHAMPION clinical trial sub-analysis was to evaluate if PA pressure-guided therapy reduced HF hospitalizations in a cohort of patients with comorbid chronic obstructive pulmonary disease (COPD, n=187).
- Reductions in PA pressure were analyzed using an area under the curve (AUC) methodology.
- There was an overall reduction in PA pressures: patients in the treatment group (n=91) had an average AUC reduction of 202 mmHg days compared to the increase of 107 mmHg days in the control group (n=96, p=0.03).

Key takeaway:
- At 15 months, there was a 41% reduction in HF hospitalization rates in the treatment group vs. control (0.55 vs. 0.96, HR 0.59, 95% CI 0.44-0.81, p=0.0009).

Respiratory Event Hospitalizations Are Reduced in Heart Failure Patients with Comorbid Chronic Obstructive Pulmonary Disease Using a Wireless Implanted Pulmonary Artery Pressure Monitoring System


- This study determined if PA pressure monitoring impacts the number of respiratory event hospitalizations (REH) in HF patients with a medical history of COPD (n=187).

Key takeaway:
- At 15 months, patients in the treatment group (n=91) had a 62% reduction in REH (0.12 vs. 0.31, HR 0.38, 95% CI 0.21-0.71, p=0.0023).
Heart Failure Hospitalizations Are Reduced in Heart Failure Patients with Comorbid Pulmonary Hypertension Using a Wireless Implanted Pulmonary Artery Pressure Monitoring System


- This CHAMPION clinical trial sub-analysis evaluated the effect of PA pressure monitoring in HF patients with comorbid pulmonary hypertension (PHTN, mean PA pressure > 25 mm Hg).
  - A total of 314 out of the 550 patients from the CHAMPION clinical trial also exhibited PHTN.
  - Patients in the PHTN cohort were further stratified by transpulmonary gradient (TPG) and pulmonary vascular resistance (PVR).
  - 67% (213/314) of PHTN patients had a TPG ≤ 15.

Key takeaways:
- At 15 months, patients in the treatment group had a 51% reduction in HF hospitalization vs. control (0.60 vs. 0.94, HR =0.64, 95% CI 0.51-0.81, p=0.0002).
- PHTN patients in the treatment group with TPG > 15 had 30% reduction in HF hospitalization vs. control (p=0.08).

Impact of Remote, Wireless Pulmonary Artery Hemodynamic Monitoring in Patients with Atrial Fibrillation and Chronic Heart Failure: Insights from the CHAMPION Trial

Miller AB, et al. JACC, 2012.19

- This CHAMPION clinical trial sub-analysis compared the baseline characteristics and impact of PA pressure-guided therapy on hospitalization rate in patients with a history of atrial fibrillation (AF, n=255) compared to those with normal sinus rhythm (n=200).
- The AF cohort had significant baseline differences compared to the sinus rhythm cohort (older: 65 vs. 59, more often male: 80% vs. 66%, more frequently had CRT or CRT-D devices: 44% vs. 27%, higher mean PA pressures: 30.2 vs. 28.5 mmHg, etc.).

Key takeaways:
- AF patients in the treatment group had a significantly lower HF hospitalization rate than those in the control group at 6 months (37%, p=0.0004) and 15 months (41%, p<0.0001).
- AF patients had a 57% higher HF hospitalization rate vs. non-AF patients (0.47 vs. 0.30 events/patient, p<0.0001).

A Wireless Hemodynamic Pressure Sensor Before and After Ventricular Assist Device Placement: A Sub-Study of the CHAMPION Trial


- This sub-analysis of the CHAMPION clinical trial evaluated the effect of PA pressure-guided therapy on optimizing medications, pump parameters and timing of ventricular assist device (VAD) intervention and transplantation in patients receiving an LVAD (n=27).

Key takeaway:
- LVAD patients who received PA pressure-guided therapy (15/27 patients) had significantly shorter times to VAD intervention (p=0.001), more changes to medical therapy based on hemodynamic information (p=0.025), and shorter times between VAD intervention and heart transplantation (p=0.001).
PA PRESSURE MONITORING ENABLES PROACTIVE AND PERSONALIZED GUIDANCE OF MEDICATION MANAGEMENT IN HF PATIENTS

Medication management is a challenging aspect in the overall treatment strategy for chronic HF patients. The range of effective medication doses for each patient varies widely and may change frequently over the course of treatment. The following sub-analyses show that PA pressure monitoring may provide early and reliable assessment of volume status and feedback on treatment response, enabling clinicians to tailor optimal medication strategies for patients suffering from chronic HF.

Medical Management Guided by Pulmonary Artery Pressures in NYHA Functional Class III Heart Failure Patients

Costanzo MR, et al. Journal of Cardiac Failure, 2011.21

- This CHAMPION clinical trial sub-analysis closely compared the medical management strategy of the treatment and control groups.
- By 6 months, dosage increases of ACE/ARB, beta blockers and nitrates were greater in the treatment group than in the control group (0.11 vs. 0.00 change in fraction of maximal dose for ACE/ARB, p=0.0042; 0.07 vs. 0.01 change in fraction of maximal dose for beta blockers, p=0.0481; 17.5 mg vs. 3.7 mg dosage change for nitrates, p=0.0422).
- Although diuretics were the most frequently adjusted drugs, at 6 months the total diuretic dose was similar between groups (p=0.1214).

Key takeaway:

- The PA pressure guided management required <1 incremental medication changes per patient per month (1.55 vs. 0.65 changes/patient/month, p<0.0001).
- The decreased HF hospitalization rate in the treatment group may be due to proactive titration of medical therapy guided by PA pressure measurements provided by the CardioMEMS HF System.

Diuretic Use Guided by a Wireless Implanted Pulmonary Artery Pressure Monitoring System in NYHA Class III Heart Failure Patients: Observations from the CHAMPION Trial


- This CHAMPION clinical trial sub-analysis study determined if adjustments to diuretic therapy in response to wireless PA pressure monitoring were associated with reduced HF hospitalization rates (n=550).
- At baseline, a similar percent of HF patients in control (n=280) and treatment (n=270) groups were receiving diuretics (91.9% and 94.2%, respectively).
- At 6 months, diuretics were more frequently adjusted in the treatment group than the control group (1,267 vs. 498 times, p<0.0001).
  - 49.7% (629/1267) of the adjustments in 57.4% (155/270) of the patients resulted from detection of increasing PA pressures.
  - 75.4% (107/142) of the changes in 17% (46/270) of those patients occurred after detection of declining PA pressures.
- The 89 treatment patients with increased loop diuretic dose had a lower rate of HF hospitalizations than the 68 control patients with similarly increased diuretic doses (0.32 vs. 0.70, p=0.0014).
  - HF hospitalization rates were similar in the 134 treatment and 173 control patients without diuretic dose changes (0.28 vs. 0.27, p=NS).

Key takeaway:

- Wireless, remote PA pressure monitoring enables physicians to effectively increase and decrease diuretic doses in HF patients, resulting in reduced HF hospitalization rates.
References


